3. Age (beyond early childhood) and sex seem to have no influence upon the coagulation time.
4. A diurnal variation does not seem to occur; possibly there is a slight increase in coagulability as the day advances, but this is probably due to experimental error.
5. There appears to be a slight tendency to decrease in the coagulability some two hours after a meal, but it is too slight to put much weight upon.
6. Calcium lactate does not appear to have any marked influence upon the coagulation time of the blood of normal individuals.
7. Citric acid appears to have a slight retarding influence upon the coagulation.
8. Considerable variation occurs in the coagulation time of a healthy individual from time to time, the nature of which is not evident.

I wish to express my gratitude to my colleague, Professor T. G. Brodie, for much valuable advice and assistance, both as regards the work and in the preparation of the charts.

NOTE.—Since writing this paper my attention has been drawn to two papers by K. Kottmann[9] upon the measurement of the coagulation time of the blood. He uses a *Thermos* bottle as a thermostat, and describes two methods. One is that of Vierordt, published in 1878, with the addition of the *Thermos* bottle to regulate the temperature. The other is a new and elaborate method, in which the *Thermos* bottle is also used with the same object.

THE CLINICAL SIGNIFICANCE OF TRANSITORY DELIRIUM CORDIS.

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THE clinical studies of irregular heart action which have been reported during the past eight years have shown the great importance of the type of irregularity which has been variously designated as auricular paralysis (Mackenzie), permanent irregularity (Hering), absolute irregularity (Hewlett), and nodal rhythm (Mackenzie). The many names proposed indicate the unsatisfactory condition of our physiological knowledge of this arrhythmia, and yet the irregularity itself has certain clinical features which distinguish it from all others. The most important of these are: (1) Its permanency in well established cases, (2) a tendency to extreme irregularity or delirium cordis, and (3) an absence of the auricular waves preceding the ventricular waves on the apex tracing, the venous pulse, the œsophageal cardiogram, and the electrocardiogram. During the past five years several writers have noted that irregularities may occur which resemble the typical permanent irregularity except for the fact that they are of a transitory character, and some of these authors believe that such transitory attacks of extreme irregularity may precede the development of the permanent form. For example, Mackenzie[1] details several case histories in which "nodal rhythm" was succeeded by normal rhythm, but later became permanent. He also describes a certain type of paroxysmal tachycardia as a transitory "nodal rhythm," but the analogy of this to typical permanent irregularity is less close than is the case in paroxysmal delirium cordis. Hewlett[2] mentions a case in which the permanent irregularity was preceded by what seemed to be an attack of delirium cordis. On the other hand, several authors who have described transitory delirium cordis fail to relate it to the permanent type of irregular heart action. This was true of Cushny and Edmunds,[3] Fr. Müller,[4] Bard,[5] and Hornung,[6] although the latter mentions a case in which the final attack lasted from October 20 to December 13, at which date the patient was discharged with his heart still irregular. It seems probable that in this case the change to a permanent irregularity had occurred under observation.

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[9] Ztschr. f. klin. Med., 1910, lix.

It is obvious that if transitory irregularity tends to become permanent, it is a matter of both theoretical and practical importance. Of theoretical importance, because the study of such paroxysms might be expected to throw light on the nature of the permanent form of irregularity; of practical importance, because of the necessity for a more guarded prognosis and for greater care in protecting the patient from influences which might hasten the development of the permanently irregular pulse. The criteria by which one may recognize the attacks of delirium cordis to which I wish to draw attention are: (1) Extreme irregularity, and (2) an absence of the auricular waves on the venous pulse preceding the ventricular waves. Between attacks the pulse is perfectly normal in rhythm and in the form of the venous tracing. The first of the above criteria distinguishes paroxysmal delirium cordis from paroxysmal tachycardia, though the two have some features in common. The second distinguishes it from irregularities due to the frequent occurrence of extrasystoles, in which a normal succession of venous waves can usually be found in many parts of an ordinary tracing.

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[1] Diseases of the Heart, 1908, p. 315.

[2] Clinical Observations on Absolutely Irregular Hearts, Jour. Amer. Med. Assoc., 1908, li, 655.

[3] Paroxysmal Irregularity of the Heart and Auricular Fibrillation, Amer. Jour. Med. Sci., 1907, cxxxiii, 56.

[4] The Nervous Affections of the Heart, Arch. Int. Med., 1908, i, 1.

[5] Des divers types d'arythmie cardiaque observés en clinique, Semaine méd., 1909, xxix, 49.

[6] Ueber atypische tachycardische Paroxysmen, Deut. Arch. f. klin. Med., 1907, xci, 469.

Two of my cases (I and II) have already been reported as instances of paroxysmal irregularity; their further history is of interest in the present discussion. Five of the six were observed at the University Hospital of the University of Michigan, the other being a private case under Dr. Hewlett's care. With the exception of Case I, venous tracings were obtained during the irregular and the regular heart action in each case.

CASE I.—*History of paroxysms of irregularity over many years; first tracings taken after operation; heart apparently normal between paroxysms; paroxysms very frequent and of short duration, ultimately becoming permanent; myocardial insufficiency.* (Case reported by Cushny and Edmunds in 1905.)

Mrs. H., aged sixty-four years, was admitted to the University Hospital December 23, 1901, for ovarian fibroid. She was operated upon December 24. Anesthesia (ether) for one hour and twenty minutes. Her condition at the end of the operation was good; pulse beats 90 per minute with no indication of irregularity. There was persistent nausea until the 27th. On the 25th and 26th the pulse rate varied between 90 and 100, with frequent periods of irregular action, as noted by the nurse. On the 27th there were three irregular paroxysms, at 8 A.M., 2 P.M., and 8 P.M., when it was impossible to obtain accurate counts at the radial. On the 28th, and also on the 29th, frequent tracings were taken at the radial with a Jacquet sphygmograph. These showed distinct periods of irregularity, lasting in some cases only a few minutes, and then the heart suddenly would become regular again. On December 30 the nausea and vomiting stopped, with a general improvement. The irregular periods became less frequent and were confined almost entirely to the night. The patient would wake up suddenly, and the heart at once became very irregular. On January 11 the heart was very irregular during the night, but became regular toward morning, and remained so until January 18, when she was discharged. The patient reported back to the hospital that the night following her discharge the heart action was very irregular.

The tracings taken during these paroxysms of irregularity, while they lack the confirmatory evidence of the venous pulse, show a typical delirium cordis. A number of large pulsations occurred at irregular intervals, and had interspersed among them smaller pulsations, sometimes singly, at other times in twos or threes or in groups of larger numbers.

The patient stated that she first noticed the irregularity twenty years before, during an illness, and that since then it had occurred whenever she was ill, excited, or exhausted. Vomiting, to which she was occasionally subject, was always followed by irregularity. The tendency to irregularity seemed to increase about ten years before the operation, as she observed that less important occasions would give rise to it than previously.

Examination of the heart during the patient's stay in the hospital showed no enlargement of cardiac dulness, no murmurs, and no objective signs of embarrassed circulation either during the irregular periods or in the regular intervals between. Clinically, then, nothing was found but alternating periods of regularity and irregularity, with no symptoms of heart failure during the irregularity nor any apparent lesion in the heart itself which might be responsible for this sudden inception of an abnormal rhythm.

In 1905 a letter was received from the patient stating that for two years after the operation she suffered very little from her heart, but then some overexertion gave rise to cardiac irregularity again, and for the last year very slight exertion or exposure to heat or cold has induced an attack.

The patient was seen on December 7, 1909, at which time she stated that she had been suffering from serious heart symptoms for some time, and that her heart was now continuously irregular. A few years before she had had sudden pain about the heart, and in the left shoulder, and she had since had more or less pain in both arms. She was now more or less continually short of breath, this becoming worse if she was tired or excited, and was also worse on exertion. At times the shortness of breath came on in spells. She had smothering attacks at night, at which times she felt that she could not get her breath and had to sit up. When walking, she frequently got dizzy and things became black before her face. One year before her feet were badly swollen, but this had practically disappeared. She did not take cold easily. She had gradually been losing weight and her appetite was variable.

Examination at this time showed an emaciated woman, inclined to dyspnœa on slight exertion. The apex beat was in the fifth intercostal space in about the mammary line. The right border of the heart was 1 cm. to the right of the sternal margin. There were no heart murmurs. The second sounds were of normal intensity. The heart action was very irregular. The arteries were thickened and tortuous. The liver was moderately enlarged and tender to the touch. The tracings taken on this date showed the typical features of a permanent irregularity.

CASE II.—*Mitral stenosis; first paroxysm observed after influenza; later ones induced by excitement or exertion; about seven paroxysms in five months; ultimately became permanent; numerous emboli, which finally caused death.* (Case reported by Dr. Hewlett.)

Mrs. B., aged fifty-five years, was first seen in February, 1908. Her family history was negative. She had never had acute articular rheumatism. In June, 1906, she had been treated for "heart disease," which had become so bad a month later that she had been unable to sleep in a recumbent position on account of dyspnœa. Since then she had had several breaks in compensation, with dyspnœa, cardiac distress, and at times slight œdema. In the intervals the compensation had been fairly good. When first seen, there had been an epidemic of influenza in the household, and she was suffering from the usual symptoms of this infection. In addition, she presented the typical signs of a mitral stenosis.

Examination at this time showed a pulse of 80 per minute and perfectly regular. The mitral stenotic murmur was of a marked presystolic type, with little if any rumble in early diastole. Three days later, after her temperature had fallen to normal, she complained of precordial distress, and felt unusually weak. The heart action was found to be absolutely irregular and about 102 beats per minute. The mitral murmur had completely changed its character. Its presystolic accentuation had disappeared and it was now loundest just after the second sound, and in the longer diastolic intervals it practically disappeared before the occurrence of the first sound. The following morning the heart action was again perfectly regular and 85 beats per minute, and the murmur had returned to its customary presystolic type. The precordial distress and general weakness had passed away.

In the next five months the patient had about seven of these paroxysms of cardiac irregularity, in three of which tracings were made which showed the characteristic absence of *a* waves. These attacks seemed to begin abruptly and were induced especially by emotional disturbances, that is, by seeing a dog nearly run down by a street car. Other attacks seemed to follow physical exertion. The attacks usually lasted during the day and passed off during the following night, the termination being associated with sweating. During the paroxysms the patient felt weak, short of breath on exertion, and suffered considerable distress from cardiac palpitation. Examination of the heart during paroxysms showed a slight enlargement of the cardiac dulness and the change in the diastolic murmur already described. Between attacks her venous pulse was of the normal type, with fairly prominent auricular waves.

In the latter part of May, 1909, the heart action became absolutely irregular, and the murmur permanently changed to the character it had shown during the former paroxysms. There was marked dyspnœa on exertion, with considerable cardiac distress, the general symptoms being less, however, than they were during the transient periods of irregularity. Death occurred by embolism of the abdominal aorta and gangrene of the legs.

CASE III.—*First paroxysms oberved after anesthesia; heart apparently normal between attacks; occasional paroxysms for several months, after which the irregularity became permanent, and the patient showed the symptoms of myocardial insufficiency. Death.*

Mr. P., aged sixty years, entered the surgical clinic of the University Hospital on October 8, 1908, and was operated upon on the 10th for a hydrocele. Very shortly after coming out of the anesthesia he developed a marked cardiac irregularity, and was immediately transferred to the medical ward. The history which was later taken threw no light on the condition, the family and personal history being in every respect normal. Tracings showed a well-marked delirium cordis, with no "*a*" waves on the venous pulse (Fig. 1). During the attack the patient was obliged to sit propped up in bed in order to avoid a most distressing dyspnœa. The heart outlines during the attack differed in no respect from those present on his admission to the surgical service. There were no murmurs either at the base or apex. The first sound at the apex was faint, but distinct and somewhat muffled; the second sound weak. The aortic second sound was of about the same intensity as the pulmonic second. On the following day the pulse became regular, and tracings showed a perfectly normal picture (Fig. 2), but on the 12th the pulse again became irregular and the tracings were the same as those taken shortly after his admission to the medical ward. He had several paroxysms during his stay, but on being placd on digitalis these attacks ceased, so that he was discharged on October 17 with a regular heart action and apparently well. Letters from the physician who later attended him, Dr. Backus, of Fayette, Ohio, stated that early in December, following several more paroxysms, the pulse became permanently irregular. On June 4, 1909, he was readmitted to the hospital with a permanently irregular heart of the ventricular type, as shown by venous tractings (Fig. 3). His shortness of breath was much in-

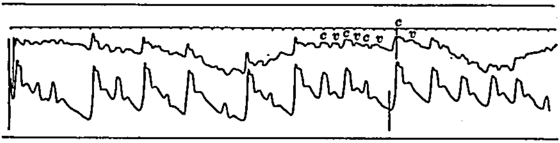

FIG. 1.—Case III. Paroxysm of irregularity on October 11, 1908. No auricular waves on the venous tracing.

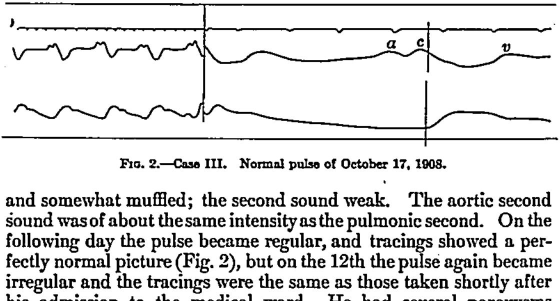

FIG. 2.—Case III. Normal pulse of October 17, 1908.

creased, there was some cyanosis, with a very troublesome cough, but no essential change in the outlines of the heart. The apex beat was now of a very heaving character, spreading over the entire precordium. He left the hospital a week later very little improved and the heart action still showing the characteristics of a permanent delirium cordis. He died a few months later.

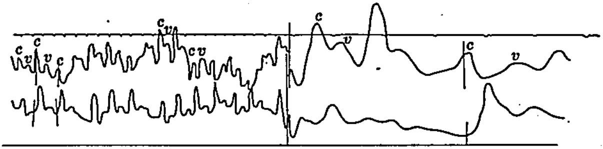

Fig. 3.—Case III. Tracing during the permanent irregularity, June, 1909.

Case IV.—*Emphysema; myocardial insufficiency, with enlarged heart; only one paraxoysm observed, then became permanent.*

Mr. W., aged fifty-nine years, was admitted to the out-patient medical clinic on January 6, 1907, complaining of shortness of breath on exertion, swelling of the lower extremities, and a very severe persistent headache. The family history was negative except for a vague account of cardiac trouble in the parents. His personal history was negative except for occasional swelling of the feet in the evening and periodic headaches, for which he had taken large quantities of acetanilide. For the last seven years these symptoms had progressively increased.

Examination: Thorax short, round, approaching a barrel-chest type. Slight cyanosis of head and extremities. No apparent dyspnœa. Veins of arms and chest full, neck veins not prominent, systolic pulsation not marked. Percussion showed heart boundaries apparently not enlarged. Apex beat poorly seen, felt in the fourth intercostal space inside nipple. At apex, first sound distant, muffled, followed by prolonged rather harsh blowing murmur transmitted outward but not upward. Murmur not heard in axilla or back. Sounds at base very feele, aortic scarcely audible, radial fairly full and rather compressible, artery moderately thickened. Systolic pressure, 115; diastolic, 75 mm. Hg. Venous tracings taken at this time showed a regular heart with well-marked "*a-c-v*" rises on the venous pulse.

On the 11th of the same month he returned to the clinic complaining of another attack of intense headache, rapid pulse, and palpitation of the heart. On examination, there was nothing marked except the extreme irregularity of the radial pulse and slightly increased cyanosis. Tracings taken showed a typical delirium cordis, with the ventricular type of venous pulse.

On the 15th he was seen at his home, and apparently had completely recovered from his attack. The pulse was perfectly regular, both as to rate and intensity, and the subjective symptoms were those present on his first visit to the hospital.

He returned to the clinic on March 1 with a partial return of the symptoms which he had had on January 11, the dyspnœa being a little less, but with marked swelling of the feet. The pulse at this time showed no abnormality.

On December 12, 1909, he was seen again. He complained of dyspnœa on unusual exertion, spells of nervousness, and occasional palpitation, but on the whole he felt better than he had at any time during the past year. More tracings were taken, which showed the positive pulse, with a fairly well-marked irregularity of the radial. He said that his pulse had been irregular ever since he was last seen (March 1, 1907).

CASE V.—*Arteriosclerosis; myocardial insufficiency, with enlarged heart; numerous paroxysms observed; later became permanent.*

Mr. S., aged sixty-eight years, was admitted to the medical clinic of the University Hospital, April 9, 1909, suffering from weakness, palpitation, and shortness of breath on exertion. His family and past history were negative, except for several slight attacks of inflammatory rheumatism at an early age. The trouble which brought him to the hospital began about two years previously as gradually increasing weakness and inability to undergo any exertion without a consequent period of breathlessness, which sometimes assumed such proportions that the patient became very much alarmed. His weight dropped during the winter over forty pounds, and was gradually going down during the early spring. He found that while in bed the palpitation of the heart was much lessened, and as a consequence he had been more or less in a recumbent position for a month or so. The examination showed an emaciated man with wasted musculature and pale muddy complexion, and in general he presented the picture of one suffering from a severe constitutional disturbance. His apex beat was heaving in character and well localized in the sixth intercostal space just outside the mammary line and about 11 cm. to the left of the median line. The area of cardiac dulness was very difficult to outline accurately, but extended about 1 cm. beyond the right border of the sternum. The upper border was apparently in the third intercostal space, and the left boundary about 12 cm. from the middle of the sternum in the fourth intercostal space. The first sound at the apex was somewhat impure, but without any definite murmur. The pulmonic second was louder than the aortic second, but neither was markedly accentuated. There was marked beaded sclerosis of the radials, and hard, tortuous brachials and temporals. When the patient first came to the hospital his pulse was regular as to rate and intensity of beat, but on the third day after admission it was noticed to be extremely irregular and intermittent. Before the apparatus could be prepared to take tracings from the radial, this irregularity had disappeared, and when the tracings were finally taken, they showed a perfectly regular action, the rate being about 98 to the minute, with well-marked *a* waves on the venous record. On the 14th the pulse again bacame slightly intermittent, and while the apparatus was being applied to his wrist the heart became extremely irregular and remained so while two tracings were taken (Fig.4), and then quite suddenly and without any apparent cause became perfectly regular again (Fig. 5). Several other sets of tracings were taken during the regular and irregular intervals (Fig. 6). In each case when the cardiac action was regular we had a normal inception of the rhythm, the *a* wave slightly preceding the ventricular systole, with the *c* and *v* waves following in order, while the tracings taken during the periods of irregularity showed the ordinary characteristics of the absolutely irregular heart—no *a* wave whatever, and the large *c* and *v*

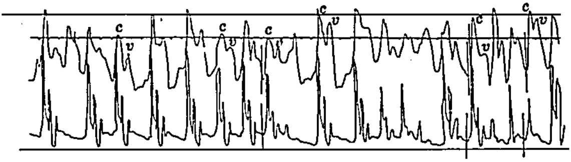

Fig. 4.—Case V. Attack of delirium cordis on April 14. Note that the venous pulse is of the positive type, beginning almost simultaneously with the radial.

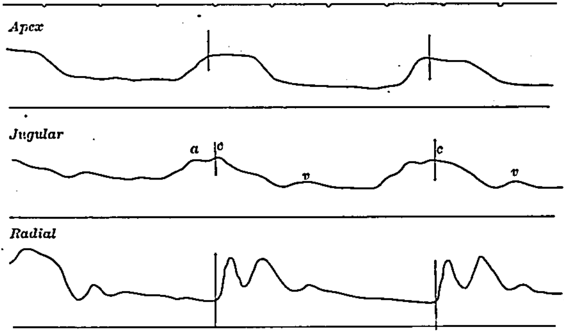

Fig. 5.—Case V. Taken a few minutes after Fig. 4. Note that the pulse is now regular and that the venous pulse begins distinctly earlier than in Fig. 4, owing to the presence of an auricular wave.

waves which occur in this condition. During the paroxysms of irregularity he showed pronounced dyspnœa, with some slight cyanosis and all the subjective symptoms of an embarrassed circulation. On closer questioning, he stated that he had had several attacks of a like character previous to his admission. He was discharged on April 16, his heart action being perfectly regular at the time. Dr. Hargrave, of Palo, Michigan, who attended him on his return home, stated in a letter received November 24, 1909, that the arrhythmia has now become permanent, with a change for the better, however, in the subjective symptoms under complete rest and large doses of strychnine sulphate.

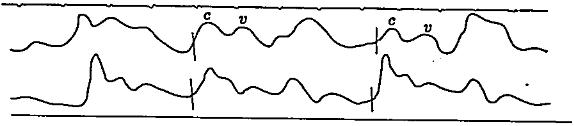

Fig. 6.—Case V. Tracing during the irregularity of April 15. The pulse is very irregular and the auricular waves are absent.

Case VI.—*Several paroxysms of irregularity following operation; heart apparently normal between attacks; up to present has remained regular.*

Mrs. H., aged forty-two years, was admitted to the gynecological service of the University Hospital in October 29, 1909, suffering from carcinoma of the uterus. There was nothing in her family or personal history which caused any suspicion of cardiac trouble, but on November 4, two days after operation, her pulse became very irregular and intermittent. This was unaccompanied by any symptoms on the part of the patient, and as it lasted only a few hours, no particular notice was taken of it. She had another period of irregularity on the 6th, which was very transitory, but on the 7th, upon the appearance of the irregularity, tracings were taken which showed a moderate degree of irregularity of the radial pulse, with a marked ventricular venous tracing (Figs. 7 and 8). The heart, when examined on her admission to the hospital, was perfectly normal in every respect; no enlargement and no murmurs. An examination of the heart was made and an orthodiagram taken during this period of irregularity, but no abnormalities other than the arrhythmia could be detected. At no time during any of the paroxysms did she complain of any distress, nor could she remember ever having had any irregularities previous to the present one. Ten days later she was discharged from the service, her pulse in the meantime remaining perfectly regular, the tracings taken showing no change from the normal whatever.

REMARKS. We have, then, six cases of transitory irregularity. Venous tracings were taken in five of these, and they showed the typical absence of *a* waves during the paroxysms and perfectly normal tracings during the periods of regular heart action. Five of these cases subsequently became permanently irregular, and the sixth was observed for too short a period to be certain that it, also, would not become permanently irregular in time. Venous tracings taken after the pulse had become permanently disorderly showed the ordinary characteristics of that condition.

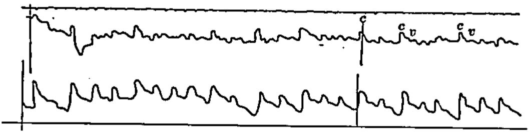

FIG. 7.—Case VI. Paroxysm of delirium cordis on November 7.

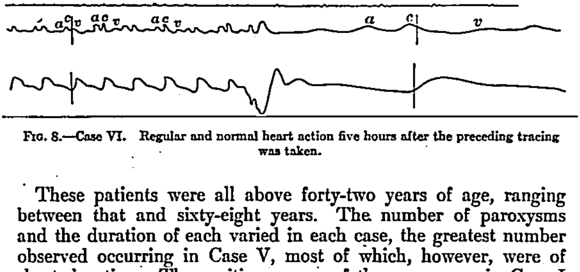

FIG. 8.—Case VI. Regular and normal heart action five hours after the preceding tracing was taken.

These patients were all above forty-two years of age, ranging between that and sixty-eight years. The number of paroxysms and the duration of each varied in each case, the greatest number observed occurring in Case V, most of which, however, were of short duration. The exciting causes of the paroxysms in Case I were several—excitement, exhaustion, and vomiting being the most prominent. Emotional disturbances in Case II would frequently bring on attacks of irregularity, although she, too, like the preceding, would suffer a paroxysm when she became unusually exhausted. The attacks in the remaining cases came on from no apparent cause, some of the paroxysms in Case V occurring while he was resting quietly in bed. Two of the cases developed their first irregularity after operation, neither one of which revealed any abnormal cardiac condition on initial examination. The time which elapsed between the first observed attack of irregularity and the establishment of a permanent delirium cordis could not be ascertained very definitely in each case, but the longest observed time was approximately fifteen months and the shortest three months. Case I, however, believed that she had had such attacks for twenty years.

Physical examination of the heart showed one case of mitral stenosis. Two patients had large hearts with myocardial insufficiency on the first examination, one of these having a systolic murmur presumably due to a relative mitral insufficiency. In the remaining three there were no abnormal signs previous to the first attack or between the paroxysms, but later, when one of these became permanently irregular, the heart was slightly larger. In Case VI the orthodiagraph showed no change in the size of the heart during a paroxysm.

The nature of this irregularity is still a matter of conjecture. In all these cases the attacks developed and ceased suddenly. This, together with the complete change in the character of the venous pulse, leads one to assume that in some way an abnormal inception of the cardiac rhythm had occurred. Two main theories as to the nature of this abnormal rhythm are held at present. These are: (1) The "nodal rhythm" of Mackenzie, and (2) auricular fibrilation (Cushny and Edmunds, Lewis,[7] Rothberger and Winterberg[8]). According to the first theory, these attacks of transient irregularity are caused by a change in the point at which the cardiac rhythm is initiated, shifting from the remains of the sinus venosus to the persisting portion of the primitive tube farther down, that is, the auriculo-ventricular node. When this occurs, the impulses travel both ways, up and down the His bundle, with a consequent simultaneous contraction of auricles and ventricles. According to the auricular fibrillation theory, the auricles pass into a state of fibrillation. In this condition coördinate auricular contractions cease and the separate portions of the muscle fibrillate, so that as an organ the auricles have ceased to beat and remain practically motionless. In this way an irregular discharge of impulses from auricles to ventricles occurs, and the ventricles beat in a more or less disorderly manner, with no evidence on the venous tracing of any auricular contractions.

CONCLUSIONS. Of six patients in whom transient attacks of delirium cordis were observed, five eventually developed the permanent type of irregularity. Many features of the attacks themselves would suggest a nervous condition, especially the onset under excitement and the complete recovery between attacks with no demonstrable heart changes. The prognosis, however, should be guarded and efforts made to avert the onset of permanent irregularity, which is practically always accompanied by symptoms of cardiac insufficiency.

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[7] Auricular Fibrillation: A Common Clinical Condition, Brit. Med. Jour., November 27, 1909, p. 1528.

[8] Vorhofflimmern und Arythmia perpetua, Wien. klin. Woch., 1909, xxii No. 24.

ERYTHREMIA OR POLYCYTHEMIA WITH ENLARGED SPLEEN AND CHRONIC CYANOSIS.

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A sufficient number of cases are now on record to identify erythremia as a distinct clinical entity. Of the symptom-trinity of the disease—cyanosis, polycythemia, and enlarged spleen—the first, cyanosis, although naturally the symptom which called the attention of clinicians to the patients in most instances, is by no means a constant element in the disease. Either for this reason, or perhaps also because of the greater convenience of a binomial nomenclature, in the more recent appellations of the disease, such as, erythremia or polycythemia splenomegalica, the cyanosis is not included in the name. In the majority of cases, however, the conditions are extremely favorable to the appearance of the cyanosis or purple staining of the skin. In many cases the cyanosis is purple rather than blue, suggesting an added hyperemia. The cyanotic coloration is usually seen on the face, the hands, and feet, but in exceptional cases it may extend over the whole surface of the body.

The hypertrophy of the spleen, though less striking at first sight than cyanosis, is yet a cardinal element of the syndrome. The degree of enlargement of the spleen is very variable. In the majority of cases it is moderate, the spleen extending one or two inches beyond the costal margin. In some cases, however, it may extend to the umbilicus, or even, as in one of Reckzeh's cases, to the crest of the ilium.

A point of importance is the fact that the splenomegaly may manifest itself for a long time before the appearance of the cyanosis. In one of Saundby and Russell's cases the patient first complained of abdominal pains and headache, and a moderate enlargement of the spleen was detected. It was only seven years later that the patient presented himself with cyanosis of the face and well-marked Hippocratic fingers. This case bears out Weber's opinion that the initial phase of this disease consists of polycythemia with splenomegaly, and without cyanosis.

Polycythemia also plays an essential part in this disease. Until recently any increase in the number of red corpuscles was only known as the result of the loss of fluid from the vascular system, as in serous diarrhœa, cholera, profuse sweating, etc., or as a consequence of residence in high altitude. The first observers of this disease were, therefore, not a little astonished at the enormous increase of the red blood corpuscles which they met with in the victims of this disease.